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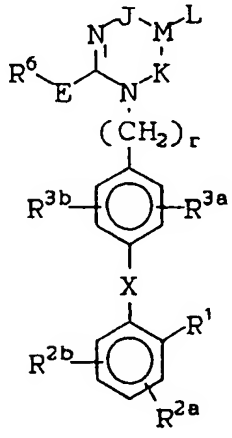
(54) Substituted pyridopyrimidinones and related heterocycles as angiotensin II antagonists.

(57) Novel substituted pyridopyrimidinones of formula (I), which are useful as angiotensin II antagonists, are disclosed.



(I)

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INTRODUCTION OF THE INVENTION

This invention relates to novel substituted pyridopyrimidinone and related heterocyclic compounds which are useful as angiotensin II antagonists in the treatment of elevated blood pressure and congestive heart failure. Thus, the substituted pyridopyrimidinone compounds of the invention are useful as antihypertensives.

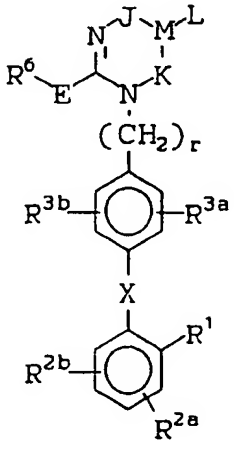
BACKGROUND OF THE INVENTION

Renin-angiotensin system (RAS) plays a central role in the regulation of normal blood pressure and seems to be critically involved in hypertension development and maintenance as well as congestive heart failure. Angiotensin II (AII), an octapeptide hormone is produced mainly in the blood during the cleavage of angiotensin I by angiotensin converting enzyme (ACE) localized on the endothelium of blood vessels of lung, kidney, and many other organs, and is the end product of the RAS. AII is a powerful arterial vasoconstricter that exerts its action by interacting with specific receptors present on cell membranes. One of the possible modes of controlling the RAS is angiotensin II receptor antagonism. Several peptide analogs of AII are known to inhibit the effect of this hormone by competitively blocking the receptors, but their experimental and clinical applications have been limited by their partial agonist activity and lack of oral absorption [M. Antonaccio. Clin. Exp. Hypertens. A4, 27-46 (1982); D. H. P. Streeten and G. H. Anderson, Jr. - Handbook of Hypertension, Clinical Pharmacology of Antihypertensive Drugs, ed. A. E. Doyle, Vol. 5, pp. 246-271, Elsevier Science Publisher, Amsterdam, The Netherlands, 1984].

Recently, several non-peptide compounds have been described as AII antagonists. Illustrative of such compounds are those disclosed in U.S. Patents 4,207,324; 4,340,598; 4,576,958; 4,582,847; and 4,880,804; in European Patent Applications 028,834; 245,637; 253,310; 291,969; 323,841; and 324,377; and in articles by A.T. Chiu, et al. [Eur. J. Pharm. Exp. Therap, 157, 13-21 (1988)] and by P.C. Wong, et al. [J. Pharm. Exp. Therap, 247, 1-7(1988), Hypertension, 13, 489-497 (1989)]. All of the U.S. Patents, European Patent Applications 028,834 and 253,310 and the two articles disclose substituted imidazole compounds which are generally bonded through a lower alkyl bridge to a substituted phenyl. European Patent Application 245,637 discloses derivatives of 4,5,6,7-tetrahydro-2H-imidazo[4,5-c]-pyridine-6-carboxylic acid and analogs thereof as antihypertensive agents.

DETAILED DESCRIPTION OF THE INVENTION

This invention relates to novel substituted pyridopyrimidinone and related heterocyclic compounds which are useful as angiotensin II antagonists, as antihypertensives, in the treatment of congestive heart failure, and in the treatment of elevated intraocular pressure. The compounds of this invention have the general formula (I):



(I)

wherein:

M is a C atom;

L is C or N when connected to K or J to form a ring as defined below;

J is -C(=Y)- where Y is 0 or NR^{21} and K and L are connected together to form a 6 membered aromatic ring containing one N atom that is not at K and five C atoms which may be substituted at the carbon atoms with R^7, R^{8a} and R^{8b};

K is -C(=Y)- where Y is 0 or NR^{21} and J and L are connected together to form a 6 membered aromatic ring containing one N atom that is not at J and five C atoms which may be substituted at the carbon atoms with R^7, R^{8a} and R^{8b} provided that only one of J or K is -C(=Y)-;

R^1 is

(a) $-CO_2R^4$,

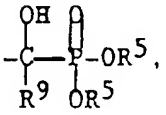
(b) $-SO_3R^5$,

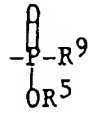
(c) $-NHSO_2CF_3$,

(d) $-PO(OR^5)_2$,

(e) $-SO_2-NH-R^9$,

(f) $-CONHOR^5$,

(g)  ,

(h) 

(i) $-SO_2NH$-heteroaryl as defined below,

(j) $-CH_2SO_2NH$-heteroaryl as defined below,

(k) $-SO_2NH-CO-R^{22}$,

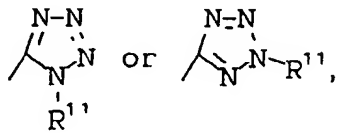
(l) $-CH_2SO_2NH-CO-R^{22}$,

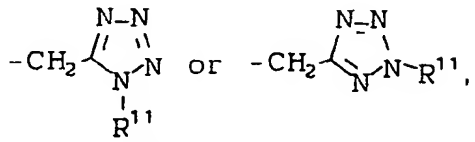
(m) $-CONH-SO_2R^{22}$,

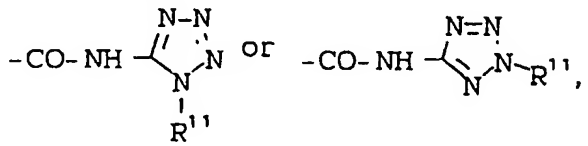
(n) $-CH_2CONH-SO_2R^{22}$,

(o) $-NHSO_2NHCO-R^{22}$,

(p) $-NHCONHSO_2-R^{22}$,

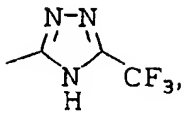
(q)  ,

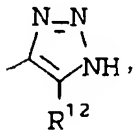
(r)  ,

(s)  ,

(t) $-CONHNHSO_2CF_3$,

(u) $-SO_2NH-CN$,

(v) 

(w) 

(x) - $PO(OR^5)(OR^4)$,

(y) - $SO_2NHCONR^4R^{22}$,

wherein heteroaryl is an unsubstituted, monosubstituted or disubstituted five or six membered aromatic ring which can optionally contain from 1 to 3 heteroatoms selected from the group consisting of O, N or S and wherein the substituents are members selected from the group consisting of -OH, -SH, -C_1-C_4-alkyl, -C_1-C_4-alkoxy, -CF_3, halo (Cl, Br, F, I), -NO_2, -CO_2H, -CO_2-(C_1-C_4-alkyl), -NH_2, -NH(C_1-C_4-alkyl) and -N(C_1-C_4-alkyl)$_2$;

R^{2a} and R^{2b} are each independently

(a) H,
(b) halogen, (Cl, Br, I, F)
(c) NO_2,
(d) NH_2,
(e) C_1-C_4-alkylamino,
(f) di(C_1-C_4-alkyl)amino
(g) SO_2NHR^9,
(h) CF_3,
(i) C_1-C_6-alkyl,
(j) C_1 -C_6-alkoxy,
(k) C_1-C_6-alkyl-S-,
(l) C_2-C_6-alkenyl,
(m) C_2-C_6-alkynyl;
(n) aryl as defined below,
(o) aryl(C_1-C_4-alkyl),
(p) C_3-C_7-cycloalkyl;

R^{3a} is

(a) H,
(b) halo (Cl, Br, I, F)
(c) C_1-C_6-alkyl,
(d) C_1-C_6-alkoxy,
(e) C_1-C_6-alkoxyalkyl;

R^{3b} is

(a) H,
(b) halo (Cl, Br, I, F)
(c) NO_2,
(d) C_1-C_6-alkyl,
(e) C_1-C_6-acyloxy,
(f) C_3-C_7-cycloalkyl,
(g) C_1-C_6-alkoxy,
(h) -$NHSO_2R^4$,
(i) hydroxy(C_1-C_4-alkyl),
(j) aryl(C_1-C_4-alkyl),
(k) C_1-C_4-alkylthio,
(l) C_1-C_4-alkyl sulfinyl,
(m) C_1-C_4-alkyl sulfonyl,
(n) NH_2,
(o) C_1-C_4-alkylamino,

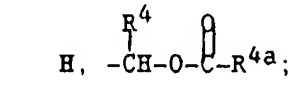
(p) di(C_1-C_4-alkyl)amino,
(q) fluoro-C_1-C_4-alkyl-,
(r) -SO_2-NHR^9,
(s) aryl as defined below,
(t) furyl,
(u) CF_3,
(v) C_2-C_6-alkenyl,
(w) C_2-C_6-alkynyl;

wherein aryl is phenyl or naphthyl optionally substituted with one or two substituents selected from the group consisting of halogen(Cl, Br, I, F), N(R^4)$_2$, CO_2R^4, C_1-C_4-alkyl, C_1-C_4-alkoxy, NO_2, CF_3, C_1-C_4-alkylthio, or OH;

R^4 is H, aryl as defined above or straight chain or branched C_1-C_6 alkyl optionally substituted with aryl or heteroaryl as defined above;

R^{4a} is aryl as defined above or straight chain or branched C_1-C_6-alkyl optionally substituted with aryl as defined above

R^5 is



E is a single bond, -NR^{13}(CH$_2$)$_s$-, -S(O)$_x$(CH$_2$)$_s$-where x is 0 to 2 and s is 0 to 5, -CH(OH)-, -O-, CO-;

R^6 is

(a) aryl as defined above optionally substituted with 1 or 2 substituents selected from the group consisting of halo (Cl, Br, I, F) -O-C_1-C_4-alkyl, C_1-C_4-alkyl, -NO_2, -CF_3, -SO_2NR^{9}R^{10}, -S-C_1-C_4-alkyl, -OH, -NH_2, C_3-C_7-cycloalkyl, C_3-C_{10}-alkenyl;
(b) straight chain or branched C_1-C_6-alkyl, C_2-C_5-alkenyl or C_2-C_5-alkynyl each of which can be optionally substituted with a substituent selected from the group consisting of aryl as defined above, C_3-C_7-cycloalkyl, halo (Cl, Br, I, F), CF_3, CF_2CF_3, -NH_2, -NH(C_1-C_4-alkyl), -OR^4 -N(C_1-C_4-alkyl)$_2$, -NH-SO_2R^4, -COOR^4, -SO_2NHR^9; or
(c) an unsubstituted, monosubstituted or disubstituted heteroaromatic 5 or 6 membered cyclic ring which can contain one to three members selected from the group consisting of N, O, S, and wherein the substituents are members selected from the group consisting of -OH, -SH, C_1-C_4-alkyl, C_1-C_4-alkoxy, -CF_3, halo (Cl, Br, I, F), or NO_2;
(d) C_3-C_7-cycloalkyl;
(e) perfluoro-C_1-C_4-alkyl,
(f) H;

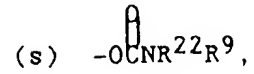
R^7 is

(a) H,
(b) straight chain or branched C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl,
(c) halo(Cl, Br, I, F) or
(d) CF_3;

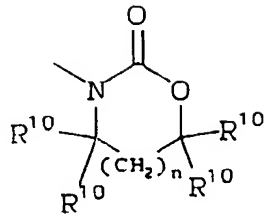
R^{8a} and R^{8b} are independently

(a) H,
(b) C_1-C_8-alkyl optionally substituted with a substituent selected from the group consisting of -OH, -guanidino, C_1-C_4-alkoxy, -N(R^4)$_2$, COOR^4, -CON(R^4)$_2$, -O-COR^4, -aryl, -heteroaryl, -S(O)$_x$-R^{22}, -tetrazol-5-yl, -CONHSO$_2$R^{22}, -SO$_2$NH-heteroaryl, -SO$_2$NHCOR^{22}, -PO(OR^4)$_2$, -PO(OR^4)R^9, -SO$_2$NH-CN, -NR^{10}COOR^{22}, -(CH$_2$)$_{1-4}$R^4,
(c) -CO-aryl,
(d) -C_3-C_7-cycloalkyl,
(e) halo (Cl, Br, I, F),
(f) -OH,
(g) -OR^{22},
(h) -C_1-C_4-perfluoroalkyl,
(i) -S(O)$_x$-R^{22},
(j) -COOR^4,
(k) -SO_3H,

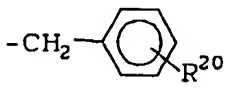
(l) $-NR^4R^{22}$,
(m) $-NR^4COR^{22}$,
(n) $-NR^4COOR^{22}$,
(o) $-SO_2NR^4R^9$,
(p) $-NO_2$,
(q) $-N(R^4)SO_2R^{22}$,
(r) $-NR^4CONR^4R^{22}$,

(s) 

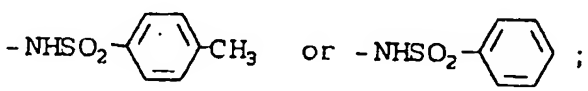
(t) -aryl or -heteroaryl as defined above,
(u) $-NHSO_2CF_3$,
(v) $-SO_2NH$-heteroaryl,
(w) $-SO_2NHCOR^{22}$,
(x) $-CONHSO_2R^{22}$,
(y) $-PO(OR^4)_2$,
(z) $-PO(OR^4)R^4$,
(aa) -tetrazol-5-yl,
(bb) -CONH(tetrazol-5-yl),
(cc) $-COR^4$,
(dd) $-SO_2NHCN$
(ee) $-NR^4SO_2NR^4R^{22}$,
(ff) $-NR^4SO_2OR^{22}$
(gg) $-CONR^4R^{22}$,
(hh)



where n=0 or 1.
R^9 is H, C_1-C_5-alkyl, aryl or arylmethyl;
R^{10} is H, C_1-C_4-alkyl;
R^{11} is H, C_1-C_6-alkyl, C_1-C_4-alkenyl, C_1-C_4-alkoxy alkyl, or



R^{12} is -CN, $-NO_2$ or $-CO_2R^4$;
R^{13} is H, (C_1-C_4-alkyl)CO-, C_1-C_6-alkyl, allyl, C_3-C_6-cycloalkyl, aryl or arylmethyl;
R^{14} is H, C_1-C_6-alkyl, C_1-C_6-perfluoroalkyl, C_3-C_6-cycloalkyl, aryl or arylmethyl;
R^{15} is H, C_1-C_6-alkyl;
R^{16} is H, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, aryl or arylmethyl;
R^{17} is $-NR^9R^{10}$, $-OR^{10}$, $-NHCONH_2$, $-NHCSNH_2$,

 ;

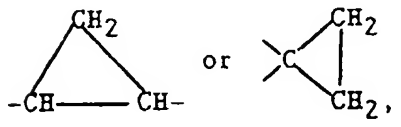
R^{18} and R^{19} are independently C_1-C_4-alkyl or taken together are $-(CH_2)_q-$ where q is 2 or 3;
R^{20} is H, $-NO_2$, $-NH_2$, -OH or $-OCH_3$;
R^{21} is
(a) aryl as defined above,
(b) heteroaryl as defined above,
(c) C_1-C_4-alkyl optionally substituted with a substituent selected from the group consisting of aryl as defined above, heteroaryl as defined above, -OH, $-NH_2$, $-NH(C_1$-C_4-alkyl), $-N(C_1$-C_4-alkyl)$_2$, $-CO_2R^{4a}$, halo(Cl, Br, F, I), $-CF_3$;
R^{22} is
(a) aryl as defined above,
(b) heteroaryl as defined above,
(c) C_3-C_7-cycloalkyl,
(d) C_1-C_6-alkyl optionally substituted with a substituent selected from the group consisting of aryl as defined above, heteroaryl as defined above, -OH, -SH, C_1-C_4-alkyl, $-O(C_1$-C_4-alkyl), $-S(C_1$-C_4-alkyl), $-CF_3$, halo (Cl, Br, F, I), $-NO_2$, $-CO_2H$, $CO_2-(C_1$-C_4-alkyl), $-NH_2$, $-NH(C_1$-C_4-alkyl), $-N(C_1$-C_4-alkyl)$_2$, $-PO_3H_2$, $-PO(OH)(O-C_1$-C_4-alkyl), $-PO(OR^4)R^9$;
(e) perfluoro-C_1-C_4-alkyl;
X is
(a) a carbon-carbon single bond,
(b) -CO-,
(c) -O-,
(d) -S-,

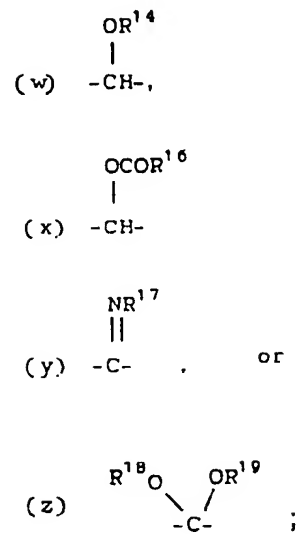
(e) $-\underset{\displaystyle R^{13}}{\overset{|}{N}}-$,

(f) $-CO\underset{\displaystyle R^{15}}{\overset{|}{N}}-$,

(g) $-N\underset{\displaystyle R^{15}}{\overset{|}{C}}O-$,

(h) $-OCH_2-$,
(i) $-CH_2O-$
(j) $-SCH_2-$,
(k) $-CH_2S-$,
(l) $-NHC(R^9)(R^{10})$,
(m) $-NR^9SO_2-$,
(n) $-SO_2NR^9-$,
(o) $-C(R^9)(R^{10})NH-$,
(p) -CH=CH-,
(q) -CF=CF-,
(r) -CH=CF-,
(s) -CF=CH-,
(t) $-CH_2CH_2-$,
(u) $-CF_2CF_2-$,

(v)  or ,



r is 1 or 2; and
the pharmaceutically acceptable salts thereof.

One embodiment of the compounds of formula (I) are those compounds wherein:

M is a C atom;

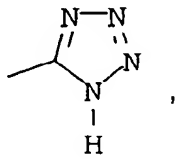
J is -C(O)-;

K and L are connected together to form a 6 membered aromatic ring containing one N atom that is not at K and five C atoms which may be substituted at the carbon atoms with R^7, R^{8a} and R^{8b};

R^1 is

(a) -COOH,

(b)



(c) $-NH-SO_2CF_3$;

(d) $-SO_2NH$-heteroaryl as defined above,

(e) $-CH_2SO_2NH$-heteroaryl as defined above,

(f) $-SO_2NH-CO-R^{22}$,

(g) $-CH_2SO_2NH-CO-R^{22}$,

(h) $-CONH-SO_2R^{22}$,

(i) $-CH_2CONH-SO_2R^{22}$,

(j) $-NHSO_2NHCO-R^{22}$,

(k) $-NHCONHSO_2-R^{22}$,

R^{2a} is H;

R^{2b} is H, F, Cl, CF_3, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, or aryl;

R^{3a} is H;

R^{3b} is H, F, Cl, CF_3, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_5-C_6-cycloalkyl, $-COOCH_3$, $-COOC_2H_5$, $-SO_2-CH_3$, NH_2, $-N(C_1-C_4\text{-alkyl})_2$ or $-NH-SO_2CH_3$;

E is a single bond, -O- or -S-;

R^6 is

(a) C_1-C_5 alkyl optionally substituted with a substituent selected from the group consisting of C_3-C_5-cycloalkyl, Cl, CF_3, CCl_3, $-O-CH_3$, $-OC_2H_5$, $-S-CH_3$, $-S-C_2H_5$, phenyl, or F;

(b) C_2-C_5-alkenyl or C_2-C_5-alkynyl; or,

(c) C_3-C_5-cycloalkyl;

R^7 is H;

R^{8a} and R^{8b} are independently

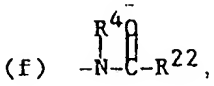
(a) H,

(b) C_1-C_6-alkyl optionally substituted with $COOR^{4a}$, $OCOR^{4a}$, OH, aryl, or $-(CH_2)_{1-4}R^4$;

(c) OR^{22},

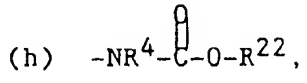
(d) -OH,

(e) $-NO_2$,



(f)

(g) $-CONR^4R^{22}$,



(h)

(i) $-NR^4R^{22}$,

(j) halo(Cl, F, Br),

(k) $-CF_3$,

(l) $-CO_2R^{4a}$,

(m) -CO-aryl as defined above,

(n) $-S(O)_x-R^{22}$,

(o) $-SO_2-NR^4R^9$,

(p) $-N(R^4)SO_2R^{22}$,

(q) aryl as defined above,

(r) $-NR^4CONR^4R^{22}$,

(s) $-N(R^4)SO_2N(R^4)R^{22}$;

X is a single bond;

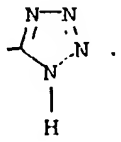
r is one.

In a class of this embodiment are those compounds of Formula (I) wherein:

R^1 is

(a) -COOH,

(b)



(c) $-NH-SO_2-CF_3$,

(d) $-SO_2NH$-heteroaryl as defined above.

(e) $-SO_2NH-CO-R^{22}$,

(f) $-CONH-SO_2R^{22}$.

E is a single bond;

r is one,

R^{2a}, R^{2b}, R^{3a} and R^{3b} are each H, $-C_1$-C_6-alkyl, $-C_2$-C_6-alkenyl, $-C_2$-C_6-alkynyl, -Cl, -F, $-NO_2$, $-CF_3$;

R^6 is $-C_1$-C_4-alkyl, -cyclopropyl, $-CH_2CH_2CH_2CF_3$, $-CH_2CH_2CF_3$, $-C_2$-C_5-alkenyl, -cyclopropylmethyl.

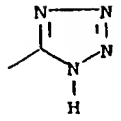
R^{8a} aid R^{8b} are each independently H, $-C_1$-C_4-alkyl, $-NO_2$, $-NR^4R^{22}$, $-OCH_3$, $-NR^4COOR^{22}$, -Cl, $-CH_2COOR^{4a}$, $-S(O)_x-R^{22}$ alkyl, $NR^4CONR^4R^{22}$, $CH_2OCO(C_1$-C_4- alkyl), NR^4COR^{22}, CO_2R^{4a}, -F, $-CH_2Ph$, $-CONR^4R^{22}$.

In a subclass are those compounds of Formula (I) wherein:

R^1 is

(a) COOH,

(b)



(c) $-SO_2NHCOR^{22}$,

(d) $-CONHSO_2R^{22}$,

(e) $-NHSO_2CF_3$;

R^{2a}, R^{2b}, R^{3a} and R^{3b} are each H, $-C_1-C_4$-alkyl, -Cl or F;

R^6 is -n-propyl, ethyl, -n-butyl, -trans-2-butenyl, $CH_2CH_2CF_3$, $-CH_2CH_2CH_2CF_3$ -cyclopropyl, -cyclopropylmethyl;

R^{8a} and R^{8b} are each independently H, $-NO_2$, $-C_1-C_4$-alkyl, $-NH_2$, $-NHCOCH_3$, $-NHCH_3$, $-S(O)_x-R^{22}$, $-N(CH_3)_2$, $-OCH_3$, -COOH, $-COOCH_3$, $-CH_2OCOCH_3$, Cl, $-CH_2COOCH_3$, $-N(R^4)CON(R^4)_2$, $-N(R^4)CO_2R^4$, $-CH_2COOH$, $-N(R^4)COR^{22}$, $-OCH_3$, CH_2OH, NHMe, CH_2Ph.

Exemplifying this subclass are the following compounds:

(1) 2-n-Butyl-1l-[(2′-carboxybiphen-4-yl)-methyl]pyrido[2,3-d]pyrimidin-4(1H)-one;

(2) 2-n-Butyl-1-[(2′-(tetrazol-5-yl)biphen-4-yl)-methyl]pyrido[2,3-d]pyrimidin-4(1H)-one;

(3) 2-n-Butyl-1-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[3,2-d]pyrimidin-4(1H)-one;

(4) 2-n-Butyl-1-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[3,4-d]pyrimidin-4(1H)-one;

(5) 2-n-Butyl-1-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[4,3-d]pyrimidin-4-(1H)-one;

(6) 2-n-Butyl-6-methyl-1-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[2,3-d]pyrimidin-4-(1H)-one;

(7) 6-Amino-2-n-butyl-1-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[2,3-d]pyrimidin-4-(1H)-one;

(8) 2-n-Butyl-1-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl-8-methyl]pyrido[4,3-d]pyrimidin-4-(1H)-one;

(9) 2-n-Butyl-1-5-methyl-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[3,4-d]pyrimidin-4-(1H)-one;

(10) 2-n-Butyl-5,7-dimethyl-1-[(2′-(tetrazol-5-yl)-biphen-4-yl)methyl]pyrido[2,3-d]pyrimidin-4(1H)-one;

(11) 6-Amino-2-n-butyl-5-methyl-1-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[2,3-d]pyrimidin-4(1H)-one;

(12) 2-n-Butyl-5-methyl-7-methylamino-1-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[2,3-d]pyrimidin-4-(1H)-one;

(13) 1-[(2′-(N-Benzoylsulfonamido)biphen-4-yl)-methyl]-2-n-butyl-5,7-dimethylpyrido[2,3-d]-pyrimidin-4-(1H)-one; and

(14) 2-n-Butyl-5,7-dimethyl-1-[(2′-(N-trifluoromethylsulfonylcarboxamido)biphen-4-yl)methyl]-pyrido[2,3-d]pyrimidin-4(1H)-one.

In a second embodiment are those compounds of formula (I) wherein:

M is a C atom;

K is -C(O)-;

J and L are connected together to form a 6 membered aromatic ring containing one N atom that is not at J and five C atoms which may be substituted at the carbon atoms with R^7, R^{8a} and R^{8b}. The class and subclass of this embodiment are the same as those described above.

Exemplifying this subclass are the following compounds:

(1) 2-n-Butyl-3-[(2′-carboxybiphen-4-yl)-methyl]pyrido[2,3-d]pyrimidin-4(3H)-one;

(2) 2-n-Butyl-3-[(2′-(tetrazol-5-yl)biphen-4-yl)-methyl]pyrido[2,3-d]pyrimidin-4(3H)-one;

(3) 2-n-Butyl-3-[2′-(carboxybiphen-4-yl)-methyl]pyrido[3,2-d]pyrimidin-4(3H)-one;

(4) 2-n-Butyl-3-[(2′-(tetrazol-5-yl)biphen-4-yl)-methyl]pyrido[4,3-d]pyrimidin-4(3H)-one;

(5) 2-n-Butyl-7-isopropyl-3-[(2′-(tetrazol-5-yl)-biphen-4-yl)methyl]pyrido[4,3-d]pyrimidin-4-(3H)-one;

(6) 6-Amino-2-n-Butyl-3-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[2,3-d]pyrimidin-4-(3H)-one;

(7) 6-Acetamido-2-n-Butyl-3-[(2′-(tetrazol-5-yl)-biphen-4-yl)methyl]pyrido[2,3-d]pyrimidin-4(3H)-one;

(8) 2-n-Butyl-5-methyl-3-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido[3,4-d]pyrimidin-4(3H)-one;

(9) 2-n-Butyl-3-[(2′-(tetrazol-5-yl)biphen-4-yl) methyl]-6-thiomethylpyrido[2,3-d]pyrimidin-4(3H)-one;

(10) 2-n-Butyl-7-carboxy-3-[(2′-(tetrazol-5-yl)-biphen-4-yl)methyl]pyrido[2,3-d]pyrimidin-4-(3H)-one;

(11) 2-n-Butyl-7-(N-isopropylcarbamoyl)amino-3-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido-[3,2-d]pyrimidin-4-(3H)-one;

(12) 2-n-Butyl-6-(N-isobutyloxycarbonyl)amino-3-[(2′-(tetrazol-5-yl)biphen-4-yl)methyl]pyrido-[2,3-d]pyrimidin-4-(3H)-one;

(13) 2-n-Butyl-6-[N-(morpholin-4-yl)carbamoyl)-N-methyl]amino-3-[(2′-tetrazol-5-yl)biphen-4-yl)-methyl]-pyrido[2,3-d]pyrimidin-4(3H)-one;